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ACCESSION NUMBER: 91019412 MEDLINE
DOCUMENT NUMBER: 91019412 PubMed ID: 2218496
TITLE: Direct interaction of a ligand for the erbB2
oncogene product with the EGF receptor and p185erbB2.
AUTHOR: Lupu R; Colomer R; Zugmaier G; Sarup J; Shepard M; Slamon
D; Lippman M E
CORPORATE SOURCE: Vincent T. Lombardi Cancer Research Center, Georgetown
University Medical Center, Washington, DC 20007.
SOURCE: SCIENCE, (1990 Sep 28) 249 (4976) 1552-5.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199011
ENTRY DATE: Entered STN: 19910117
Last Updated on STN: 20000303
Entered Medline: 19901108

AB The erbB2 oncogene encodes a 185-kilodalton transmembrane protein whose sequence is similar to the epidermal growth factor receptor (EGFR). A 30-kilodalton factor (gp30) secreted from MDA-MB-231 human breast cancer cells was shown to be a ligand for p185erbB2. An antibody to EGFR abolished the tyrosine phosphorylation induced by EGF and transforming growth factor-alpha (TGF-alpha) but only partially blocked that produced by gp30 in SK-BR-3 breast cancer cells. In two cell lines that overexpress erbB2 but do not express EGFR (MDA-MB-453 breast cancer cells and a Chinese hamster ovary cell line that had been transfected with erbB2), phosphorylation of p185erbB2 was induced only by gp30. The gp30 specifically inhibited the growth of cells that overexpressed p185erbB2. An antibody to EGFR had no effect on the inhibition of SK-BR-3 cell colony formation obtained with gp30. Thus, it appeared that gp30 interacted directly with the EGFR and erbB2. Direct binding of gp30 to p185erbB2 was confirmed by binding competition experiments, where gp30 was found to displace the p185erbB2 binding of a specific antibody to p185erbB2. The evidence described here suggests that gp30 is a ligand for p185erbB2.

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ACCESSION NUMBER: 93203131 MEDLINE
DOCUMENT NUMBER: 93203131 PubMed ID: 1688228
TITLE: The role of erbB-2 and its ligands in growth control of
malignant breast epithelium.
AUTHOR: Lupu R; Dickson R B; Lippman M E
CORPORATE SOURCE: Lombardi Cancer Research Center, Georgetown University
Medical Center, Washington, DC 20007.
SOURCE: PRINCESS TAKAMATSU SYMPOSIA, (1991) 22 49-60. Ref: 23
Journal code: 9301172.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 19930507
Last Updated on STN: 20000303
Entered Medline: 19930421

AB A wealth of recently derived information has strongly implicated the protooncogene erbB-2 (also termed HER-2 or neu) and its protein product as critically involved in human breast cancer as well as other important epithelial malignancies. Because of its substantial homology with the EGF receptor, erbB-2 has long been assumed to encode a growth factor receptor, although until recently definitive identification of ligand(s) has remained elusive. Both in a mutated form and when overexpressed in a non-mutated form, erbB-2 is capable of inducing malignant transformation of many target cells including immortalized breast epithelium. We have recently identified and purified a 30 kDa size growth factor secreted by some human breast cancer cells. The factor is related to transforming growth factor-alpha (TGF-alpha) in its ability to bind to the epidermal growth factor (EGF) receptor (though with about 10 fold lower apparent affinity), its ability to phosphorylate EGF receptor and its ability to induce cloning of normal rat kidney (NRK) fibroblasts. However, it is distinct from TGF-alpha as determined by peptide mapping and its ability to induce activation of erbB-2. TGF-alpha and EGF are incapable of directly inducing phosphorylation of erbB-2. However, in a variety of spontaneously occurring tumor cells as well as cell lines transfected with erbB-2 prepared in our laboratory, 30 kDa glycoprotein (gp30) is capable of inducing direct phosphorylation of erbB-2. The ability to induce phosphorylation of erbB-2 is not inhibited by an anti-EGF receptor blocking antibody. In cells that overexpress erbB-2, the gp30 low concentrations is stimulatory of both standard

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mitogenesis assays and in clonogenic assays. At higher concentrations, the ligand is growth inhibitory in both of these assays. Because of the ability of gp30 to compete for binding with antibodies directed against erbB-2 which inhibit growth, the gp30 ligand is capable of reversing antibody-induced inhibition of growth. In addition, the gp30 ligand can overcome inhibitory effects seen in cells which overexpress erbB-2 which are induced by extracellular domain fragments of the erbB-2 receptor, once again suggesting a specific pathway of action for the gp30 ligand mediated for interaction with erbB-2.(ABSTRACT TRUNCATED AT 400 WORDS)

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ACCESSION NUMBER: 1996:333020 CAPLUS
DOCUMENT NUMBER: 125:1367
TITLE: Methods and compositions using oncogene
product-binding compounds for cancer therapy and for
prognosticating responses to cancer therapy
INVENTOR(S): Bacus, Sarah S.
PATENT ASSIGNEE(S): Becton Dickinson Co., USA
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 767, 041,
abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5514554	A	19960507	US 1993-50113	19931007
CA 2096417	AA	19930223	CA 1992-2096417	19920821
WO 9303741	A1	19930304	WO 1992-US7117	19920821
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
EP 656367	A1	19950607	EP 1995-101046	19920821
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
IL 103250	A1	19990312	IL 1992-103250	19920922
US 5288477	A	19940222	US 1993-32529	19930315
PRIORITY APPLN. INFO.: IL 1991-99284 A 19910822				
US 1991-767041 B2 19910927				
US 1991-767042 B2 19910927				
WO 1992-US7117 W 19920821				
EP 1992-918871 A3 19920821				

AB A method is described for detg. the efficacy of a therapeutic agent, in vitro, for a cancer expressing or over-expressing an oncogene product. The method is particularly useful for detg. the efficacy of therapeutic agents that have a binding affinity for cancer that express HER-2/neu. N24, N28 and N29 monoclonal antibodies are described which have been identified by this method. One or more of these antibodies can be used as a therapeutic agent in the treatment of breast, stomach, ovarian or salivary cancers.

Untitled

ACCESSION NUMBER: 2003493281 IN-PROCESS

DOCUMENT NUMBER: 22932030 PubMed ID: 14569800

TITLE: Measuring HER-2 in breast cancer.
Immunohistochemistry, FISH, or ELISA?.

AUTHOR: Yeh I-Tien

CORPORATE SOURCE: Dept of Pathology, University of Texas Health Science
Center at San Antonio, 7703 Floyd Curl Dr, San Antonio, TX
78229, USA.

SOURCE: AMERICAN JOURNAL OF CLINICAL PATHOLOGY, (2002 Jun) 117
Suppl S26-35.

Journal code: 0370470. ISSN: 0002-9173.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: IN-PROCESS; NONINDEXED; Abridged Index Medicus Journals;
Priority Journals

ENTRY DATE: Entered STN: 20031023

Last Updated on STN: 20031023

AB Measuring HER-2 is important for selecting optimal
therapy and predicting prognosis in breast cancer patients. Current
methods for evaluating HER-2 include measuring protein
overexpression by immunohistochemistry (IHC), measuring gene copy number
by fluorescent in situ hybridization (FISH), and measuring shed
antigen in the serum by enzyme-linked immunosorbent assay (ELISA).
This review compares these 3 methods and analyzes the current literature
pertaining to this subject. In comparing IHC with FISH, the negative
predictive value is excellent for commonly used commercial antibodies but
the positive predictive value is highly variable. However, by considering
only strongly staining cases as positive by IHC, the positive predictive
value is markedly improved. ELISA is useful in the follow-up care of
patients with breast cancer. An algorithm for using all 3 methods is
presented.

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ACCESSION NUMBER: 1991:402504 CAPLUS

DOCUMENT NUMBER: 115:2504

TITLE: C-erbB-2 external domain gp75, its
preparation with recombinant cells, and its use for
immunodiagnosis or treatment of tumors

INVENTOR(S): Stuart, Susan G.; Monahan, John J.; Langton, Beatrice
Claudia; Hancock, Miriam E. C.; Chao, Lorraine A.;
Bluford, Peter

PATENT ASSIGNEE(S): Triton Biosciences, Inc., USA

SOURCE: PCT Int. Appl., 107 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9102062	A2	19910221	WO 1990-US4340	19900802
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WO 9102062	A3	19910613		
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W: AU, CA, JP

RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE

CA 2042064	AA	19910205	CA 1990-2042064	19900802
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AU 9064135	A1	19910311	AU 1990-64135	19900802
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AU 645760	B2	19940127		
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EP 444181	A1	19910904	EP 1990-914094	19900802
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EP 444181	B1	20011031		
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R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE

JP 04503012	T2	19920604	JP 1990-513165	19900802
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EP 1006194	A2	20000607	EP 1999-124820	19900802
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R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE

AT 207958	E	20011115	AT 1990-914094	19900802
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ES 2166352	T3	20020416	ES 1990-914094	19900802
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US 2002155527	A1	20021024	US 2001-769508	20010126
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PRIORITY APPLN. INFO.: US 1989-389920 A 19890804

EP 1990-914094 A3 19900802

WO 1990-US4340 A 19900802

US 1992-826231 B1 19920122

US 1993-115073 B1 19930902

AB A recombinant plasmid encoding the external domain of the c-erbB-2 protein
(gp75) is provided for manufg. (non-)glycosylated gp75

. The pure gp75, from recombinant prepn. or synthesis, and the
antibodies thereto are used in immunodiagnosis of tumors by detecting the

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antigen/antibody present in body fluid. Gp75 can also be prepd. as a vaccine against the c-erbB-2 oncogene-assocd. neoplasm. In addn., gp75 can be used in conjunction with alkylating agents in tumor chemotherapy. A 2 kb DNA encoding gp75 was cloned into an SV40-based vector to give pFRSV-c-erbB-2sec. Non-glycosylated (75 kilodalton) and glycosylated (90 kilodalton) gp75 were purified from the culture medium of the transfected CHO cells. Monoclonal antibody TAB to gp75 were prepd. and used for detection of the shed antigen in Balb/c nude mice transplanted with the c-erbB-2-transformed tumor cells NIH3T3-t. Use of the monoclonal antibody in diagnosis of human breast cancer was also described.

Untitled

ACCESSION NUMBER: 92096712 EMBASE

DOCUMENT NUMBER: 1992096712

TITLE: Characterization of a growth factor that binds exclusively
to the erbB-2 receptor and induces cellular responses.

AUTHOR: Lupu R.; Colomer R.; Kannan B.; Lippman M.E.

CORPORATE SOURCE: V.T. Lombardi Cancer Res. Ctr., Georgetown University,
Medical Center, 3800 Reservoir Road, Washington, DC 20007,
United States

SOURCE: Proceedings of the National Academy of Sciences of the
United States of America, (1992) 89/6 (2287-2291).

ISSN: 0027-8424 CODEN: PNASA6

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer

022 Human Genetics

029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The erbB-2 oncogene encodes a 185-kDa transmembrane protein that has been suggested to be a growth factor receptor. We have previously identified and purified a 30-kDa growth factor (gp30) that is a ligand for the p185(erbB-2) protein that at high concentrations induces growth inhibition of cells with erbB-2 amplification. We now report the purification and characterization of a protein from SKBr-3 human breast cancer cells with a molecular mass of 75 kDa (p75) that is a p185 (erbB-2) ligand. An affinity column coupled to the extracellular domain of p185(erbB-2) was used for the purification. We found that p75 induced tyrosine phosphorylation of the erbB-2 oncoprotein, as determined by in vivo and in vitro phosphorylation and phosphoamino acid analysis. p75, as well as gp30, stimulated cell proliferation and colony formation of cells overexpressing erbB-2. The specificity of this effect was confirmed by showing that the antiproliferative effects of soluble erbB-2 extracellular domain were reversed by either p75 or gp30. p75 did not show binding to the epidermal growth factor receptor and had no growth effects on cells overexpressing epidermal growth factor receptor. These data show that SKBR-3 cells, which exhibit erbB-2 amplification and overexpression, secrete a growth factor that binds and activates p185(erbB-2) specifically.